

Chief Scientific Adviser's Science Report

Issue five: Food allergy and intolerance



“In this fifth CSA report we focus on food allergy and intolerance. I am pleased to present the FSA’s work in this area, which I believe utilises a wide range of scientific approaches to help ensure food allergic and intolerant consumers can make safe food choices.”

Professor Guy Poppy,
FSA Chief Scientific Adviser



In developed countries, there is evidence that food allergy and intolerance is on the rise, and poses a significant problem. On average, 2 children per school class will have a food allergy and on average 10 people each year die in England and Wales as a result of having a food allergy.

The science in this area is complex, but great advances are being made to help us understand why food allergy develops and how it may be prevented. For example, significant progress has been made in understanding the influence that diet in infancy has on preventing food allergy.

However, there is still uncertainty in food allergy and intolerance and the emergence of new data needs to be considered carefully to ensure advice to consumers reflects the best available evidence.

This report begins by explaining the science behind food allergy and intolerance. We then present key pieces of research that the FSA is funding and our approach to risk assessment and management.

The report also highlights essential collaboration between the FSA and partners, both within the UK and internationally, so that together we can tackle this problem.

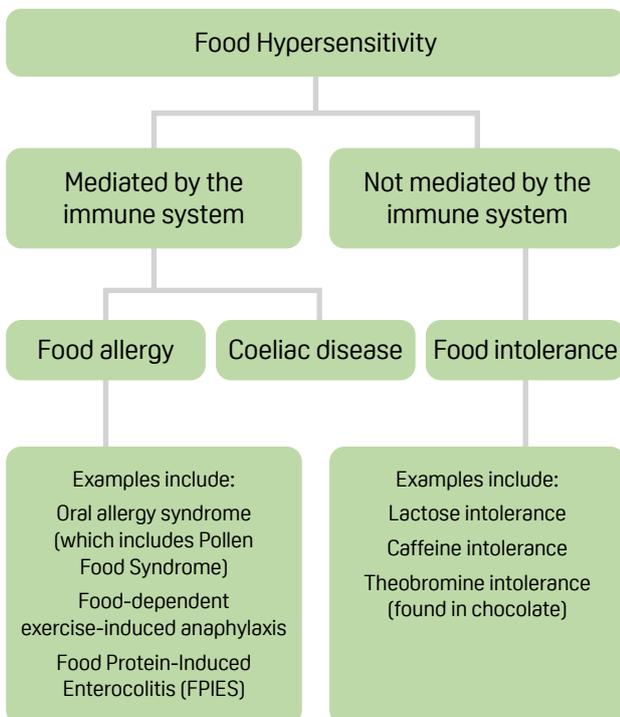
Finally, we discuss how the growing interest in insects as a potential solution for food security, may have further implications for food allergy.

Food allergy and intolerance can be a confusing subject – many people find it difficult to tell the difference between the two. In this section of the report we will explain what the differences are and the science behind why and how these adverse reactions to food occur.

What is a food allergy or intolerance?

Food allergy, food intolerance and coeliac disease are repeatable adverse reactions to foods. Together they are described by the term ‘food hypersensitivity’. Food hypersensitivity is different from food poisoning and does not include the avoidance of a food due to taste or texture, or for cultural or religious reasons.

Classification of reactions to food



Key differences between food allergy and food intolerance

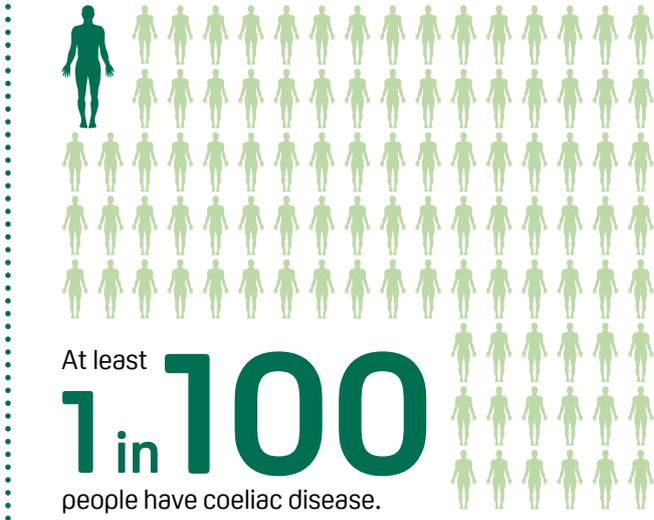
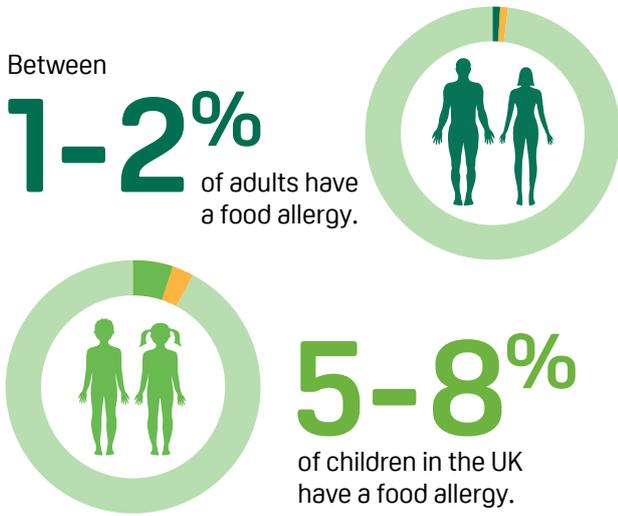
The main difference between food allergy and food intolerance is that with a food allergy the immune system responds to a particular food and causes an allergic reaction. Food intolerance is not caused or controlled by the immune system and is less well understood.

	Food allergy	Food intolerance
Time for reaction to occur	 Minutes to hours	 or Hours to days
Quantity of ingested food		
Severity of reaction	 Acute: Can be severe and life threatening	 Chronic symptoms

In autoimmune conditions the immune system mistakenly attacks and causes damage to the body. Coeliac disease is a type of autoimmune condition in which the body reacts to gluten in food and causes damage to the gut. This affects the gut’s ability to absorb nutrients from food. Gluten is found in cereals such as wheat, rye, barley and oats.

Many people find it difficult to tell the difference between food allergy and food intolerance.

Prevalence of food allergy and coeliac disease



Is food allergy getting more common?

As has been the case in North America and other countries in Europe, food allergy has become more common in the last 10-20 years in the UK. Research has also shown that the type of foods people are reacting to may be changing. Foods which are relatively new to the UK diet, like kiwi, are also being reported to cause food allergy in some people.

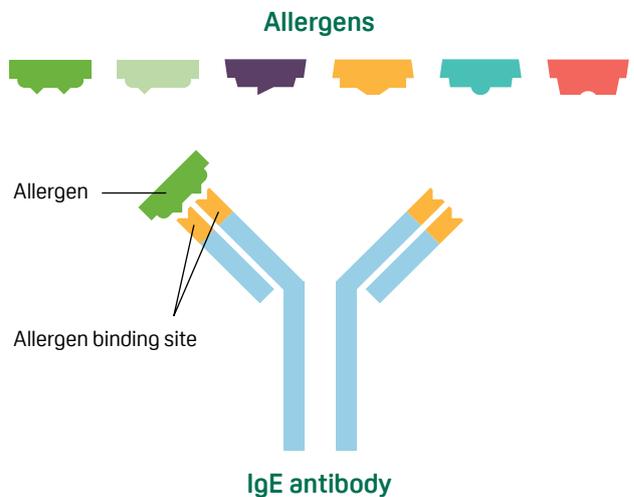
How does the immune system cause an allergic reaction to a food?

Under normal circumstances our immune system reacts only when a substance is identified as a threat, such as when an individual is exposed to viruses, bacteria, or foreign materials. However, in some cases an allergic reaction occurs when our immune system mistakenly responds to a harmless substance, like proteins found in food, as a threat.

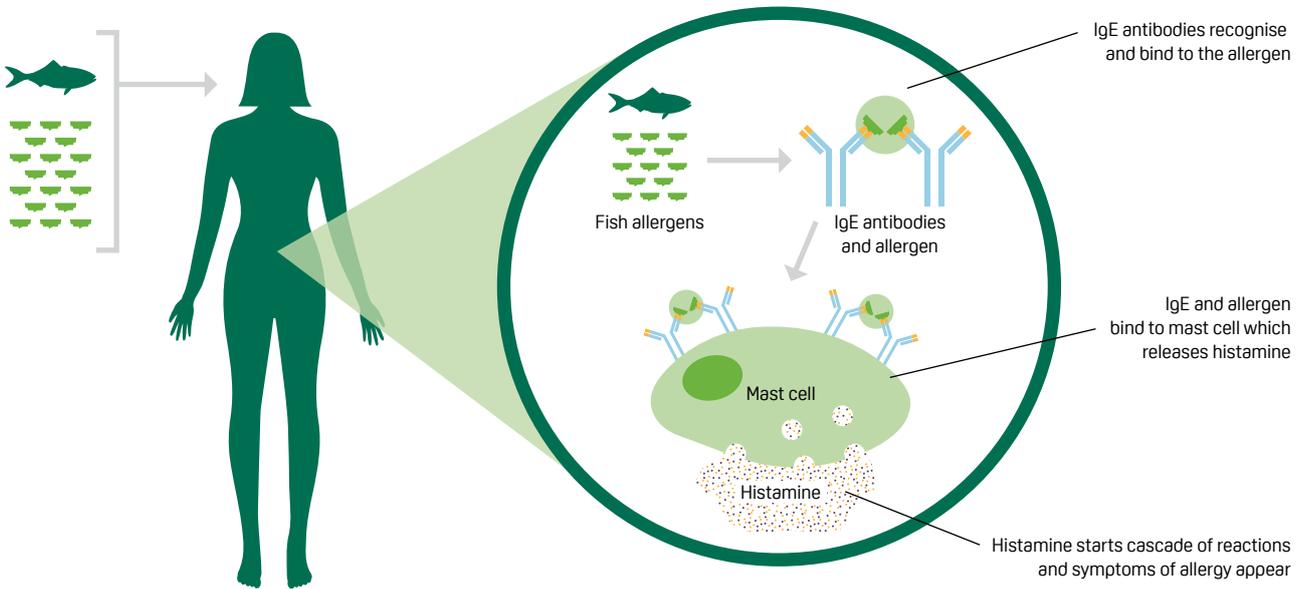
The two key players in food allergy are allergens and antibodies. Food allergens are proteins found in food which can cause

a reaction in an allergic individual. There are often a number of allergens in foods responsible for food allergic reactions; for example, there are at least 13 known allergenic proteins in peanuts.

Antibodies are responsible for detecting the allergen and presenting it to other cells in the immune system, which then leads to the symptoms of an allergic reaction. A particular type of antibody known as immunoglobulin E or 'IgE' is most commonly responsible for allergic reactions to food.



How an allergic reaction occurs



In common with all other forms of allergy, food allergy develops in two phases. The first phase is known as sensitisation. This involves exposure to an allergen, which primes the immune system to respond the next time the body encounters the same allergen. When this happens the immune system mounts a more rapid and aggressive response to the allergen.

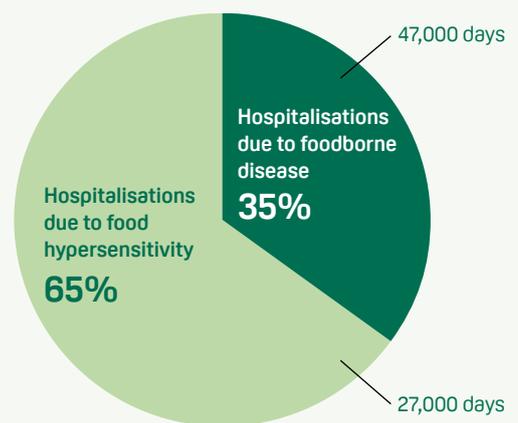
Common symptoms of food allergy and intolerance

Food allergy symptoms	Shared symptoms	Food intolerance symptoms
Swelling and tingling of lips	Nausea	Bloating
Shortness of breath	Vomiting	Fatigue
Anaphylaxis	Diarrhoea	Headache/migraine
Runny nose	Skin rashes	Joint pain
Red, itchy eyes		

There is currently no cure for food allergy and the best way to manage the condition is for someone with a food allergy to avoid the food to which they are allergic.

What is the impact of food hypersensitivity compared with foodborne disease?

Food hypersensitivity is responsible for more hospitalisations each year than foodborne disease. The total number of days spent in hospital each year, however, is greater for foodborne disease.



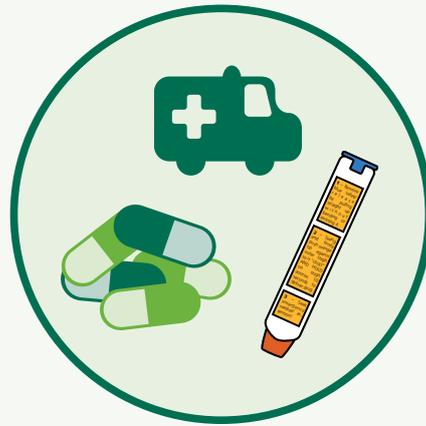
On average 10 people die each year in England and Wales from food allergy; this compares with 168 for foodborne disease. People who die from food allergy tend to be younger than those who die from foodborne disease.

What is anaphylaxis?

Anaphylaxis is a severe, life threatening allergic reaction which involves several organs in the body, particularly the heart and lungs. The symptoms need immediate treatment and include a red raised itchy rash, breathing difficulties and a dramatic drop in blood pressure, which can lead to loss of consciousness.

Many people with food allergy are prescribed adrenaline auto-injectors. These allow adrenaline to be injected easily to help treat the symptoms of an allergic reaction very quickly. Despite the severity of the reaction, deaths from anaphylaxis are rare.

There is evidence that several factors can affect the severity of an allergic reaction such as the amount of allergen eaten and in what form and whether the individual is tired, has recently exercised or has an underlying heart condition.



How are food allergy and intolerance diagnosed?

Over-reporting of food allergy is common, and surveys have found highly variable results. One UK survey found rates of self-reported food allergy as high as 15% – significantly higher than studies which report food allergy diagnosis by doctors.

Allergy tests that are available on the high street lack scientific evidence to show they work and food allergies need to be diagnosed by doctors, preferably specialists in allergy. Diagnosis commonly involves examining the individual's medical history, testing the blood for IgE antibodies or performing a skin prick test which shows what foods the body is

sensitised to. Food challenges are considered the gold standard for allergy diagnosis. During a food challenge, where the participant may or may not know what food they are eating, symptoms are closely monitored and recorded. Food challenges must be performed under close clinical supervision, so that the dose of food allergen can be carefully controlled and any symptoms can be treated quickly.

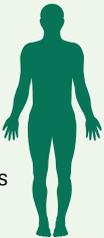
The only reliable way to diagnose food intolerance is under the supervision of a health professional, to avoid specific foods whilst keeping a diary to record exactly what is eaten and what symptoms are experienced. This will help identify what foods someone is intolerant to.

What factors affect whether someone develops food allergy?

	<p>Skin Research shows that the skin is an important factor in developing food allergy to some foods. Food allergens in the environment can enter the body through the skin and may cause sensitisation. Children with eczema are at higher risk of developing food allergy.</p>
	<p>Genetics Having one or both parents with an allergy increases the risk of food allergy.</p>
	<p>Household pets Studies suggest that having pets decreases the likelihood of developing food allergy.</p>
	<p>Diet in infancy There is emerging evidence that children who eat food allergens in early life, rather than avoiding or delaying when they are eaten, have a reduced risk of food allergy. In Israel for example, peanuts are a common weaning food and the number of children with peanut allergy is extremely low.</p>
	<p>Environment Studies report lower prevalence of food allergy in rural settings versus urban settings; this is thought to be due to the higher diversity of bugs that an individual is exposed to in a rural setting.</p>
	<p>Occupation People can develop ‘occupational allergy’, which occurs with exposure to an allergen in the workplace over a long period of time. Fishmongers, for example, can develop allergy to fish and shellfish.</p>

What foods are people allergic to?

Almost any food can trigger an allergic reaction in a susceptible individual, but some foods are more common than others. In the UK, allergy to peanuts, tree nuts (such as almond, walnut and hazelnut), wheat, cows’ milk, fish and egg are the most common. The difference in prevalence between children and adults is largely due to children having higher rates of allergy to milk and egg, which commonly resolve in later childhood. Allergy to a wider range of foods, including fruits and vegetables, are often reported in adults.

Common food allergy in childhood	Common food allergy in adulthood
<ul style="list-style-type: none"> Peanuts Tree nuts Fish Shellfish Cows’ milk Egg 	<ul style="list-style-type: none"> Peanuts Tree nuts Fish Shellfish Fruits, such as apples and peaches Vegetables 

Can people be allergic to more than one food?

Yes, many people have an allergy to more than one food. Interestingly, someone with a specific food allergy may also have an allergic reaction to a similar food or non-food allergen, such as pollen. This is because different substances can have similar proteins (allergens), which the body is unable to distinguish between. This can occur between the food that someone is allergic to and a similar protein in another food or substance. This is known as cross-reactivity. A cashew allergic person, for example, may also react if exposed to pistachio nuts.

Cross-reactivity between pollens and foods is known as pollen food syndrome and symptoms are usually mild in most people, characterised by itchiness and minor swelling of the mouth and throat. Fruit, vegetables and nuts are commonly implicated in cross-reactivity. It is possible, however, to deactivate the allergens in fruits by cooking – the intense heat alters their normal structure and the body no longer recognises the allergen.

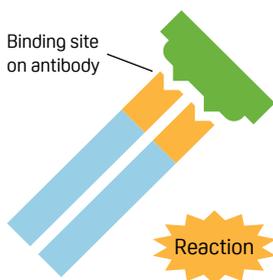
Fruit, vegetables and nuts are commonly implicated in cross-reactivity.

Examples of cross-reactive allergy

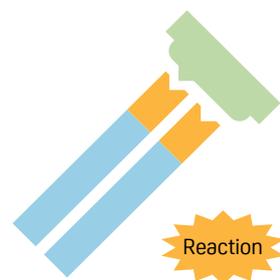
Allergies to	Might result in cross-reactive allergies to
Natural rubber latex	Avocado, bananas, chestnut, papaya and/or kiwi
Birch pollen	Almonds, apples, carrots, celery, coriander, cherries, hazelnuts, fennel, parsley, peaches, pears, plums and/or kiwi
Grass pollen	Celery, melons, oranges, peaches and/or tomatoes

Cross-reactivity

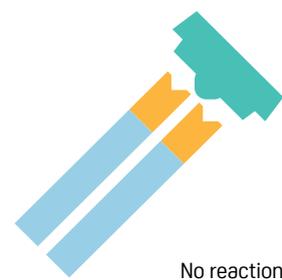
Birch pollen allergen



Apple allergen



Fish allergen



In the second section of the report, we will describe the work the FSA is taking forward to improve the lives of those with food hypersensitivity. This includes commissioning research projects and surveys, conducting risk assessments and working with government scientific advisory committees.

The Food and You survey

Food and You is the FSA's large and ongoing consumer survey of behaviours, attitudes and knowledge relating to food safety and other food-related issues. The survey conducts face-to-face interviews with around 3,000 adults in each survey.

The first wave of the survey took place in 2010, with subsequent phases run every two years. The three phases completed to date have included questions relating to food allergy.

The findings from the most recent survey in 2014 reported that:

- 4% of those interviewed said they had a food allergy
- 66% of those reporting having a food allergy said that they had seen a doctor about it
- 40% said that their allergy was clinically diagnosed, which represents 2% of respondents
- 11% of respondents said they had someone in the household with a food allergy

The next Food and You survey is taking place this year (2016), and significant questionnaire redevelopment work has taken place to provide more information on food allergy and intolerance. Findings from this survey will include information on:

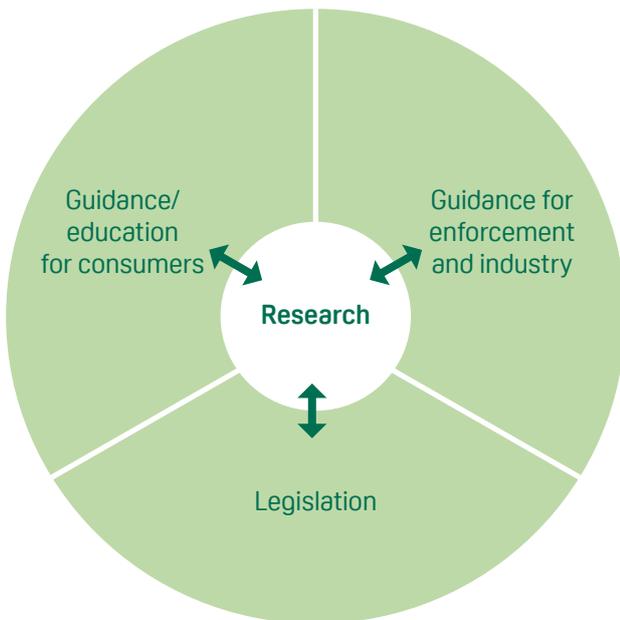
- What foods people report being allergic or intolerant to
- The age at which people first report symptoms
- The types of symptoms people report

The fieldwork for the 2016 survey has been completed and headline findings are expected to be published in early 2017, accompanied by data that will support further research on food allergy and intolerance.

4% of those interviewed said they had a food allergy.

The FSA Food Allergy and Intolerance Research Programme

For over twenty years the FSA has invested in its research programme to investigate food allergy and intolerance. The main aims of this programme have been to investigate the causes and mechanisms underlying food allergy and intolerance. The FSA commissions projects to develop an improved understanding of the important issues which consumers with food allergy and intolerance face. This helps to ensure that policies are based on robust and up to date scientific evidence.



The programme has a history of responding to emerging issues in food allergy and has been at the forefront of new research which investigates how the timing of introduction of common allergenic foods into the infant diet influences the risk of infants developing food allergy. The programme has also funded research which characterised kiwi as a new and growing food allergy, identified the skin as a probable route of exposure to food allergens leading to sensitisation, and supported work to provide robust data on determining the prevalence of food allergy in the UK.

Food allergy in adults is an emerging area of interest for the FSA, with few up to date studies available on which to base policy. Doctors are reporting that they are seeing more adults with food allergy symptoms.

Because adults have a longer history of exposure to food allergens, adult allergy is more varied, with greater diversity in foods and symptoms. Multiple factors such as medication, exercise and alcohol also play a role. The severity of reactions can also change with age, potentially due to behavioural as well as biological factors.



What projects are the FSA currently funding?

The FSA's portfolio of ongoing and recently completed projects includes:

Prevalence of Infant Food Allergy (PIFA) University of Southampton

In 2005 the PIFA study team began recruiting pregnant women from the Winchester area in Hampshire to investigate how the diet of mothers and infants influences food allergy risk.

The study has already reported findings when the children were 2 years of age. Professor Graham Roberts, who leads this study says...



“One in twenty UK infants were found to have a food allergy. The prevalence of food allergy was very different in different European countries, with cases being very rare in Greece. We identified risk factors for the development of food allergy in childhood, which may help us to prevent food allergy”

The study is now following-up the participants and is investigating their food allergy and asthma status between 8-9 years of age. The fieldwork has been completed and data are currently being

analysed, with findings to be published in early 2017. This information will help to ensure advice to consumers is based on up to date evidence which reflects emerging food allergies and will provide information on how the UK population differs from that of other European countries.

This study forms part of a Europe-wide project (Integrated Approaches to Food Allergen and Allergy Risk Management – iFAAM). Here, study investigator Dr Kate Grimshaw tells us why being part of collaborative projects is important...



“Being part of collaborative projects not only enables research results to be compared between the nations involved but also allows a pooling of the

differing expertise and experiences in all food allergy stakeholder groups. This helps to ensure any conclusions and results from the research are widely applicable across all interested parties.”

The TRACE Study

Addenbrooke's Hospital (University of Cambridge)

The TRACE study undertaken at clinical sites in Cambridge (Addenbrooke's Hospital) and London (Royal Brompton Hospital) is a randomised cross-over trial investigating exactly how much peanut is able to cause an allergic reaction in adults with a peanut allergy. It is also seeking to establish whether the amount of allergen required to cause an allergic reaction, or the severity of a reaction in an individual changes in the presence of two factors - exercise and stress (in the form of sleep deprivation).

The findings of this study will help inform work the FSA is undertaking to develop management threshold levels (or 'action levels') for the unintentional presence of allergens in food to inform labelling and when conducting risk assessments.

The study sites have recently completed their food challenges and the results of the study will be available next year.

A participant of the TRACE study says:

"I think it's important to be a part of the TRACE study because I feel I am helping future allergy sufferers to be more aware and safer when making choices in supermarkets and restaurants. It can be really frightening to have a reaction and not know what is happening or why. I have also learnt so much about my allergy and how my body reacts. I now know what my first symptoms are, and I feel I will be more likely to recognize an allergic reaction straight away, which could have prevented a very severe reaction I had a few years ago. I now know more about what to do when I have a reaction and when I should use my epipen®. I will finish knowing far more about peanut allergies and how I can be safer."



Understanding the evidence base

It is important that the FSA bases its advice on the best available evidence, so alongside commissioning research projects, we also commission reviews which tell us what the entire evidence base on a particular area says. The FSA commissioned Imperial College London to conduct a systematic review of evidence on maternal and infant diet and whether this influences whether the child develops food allergy and other allergic and autoimmune conditions. This review included the FSA-funded Enquiring About Tolerance (EAT) Study conducted at King's College London.

The systematic review was considered by one of the government's scientific advisory committees - the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT). The COT published a statement on their assessment of the evidence base in September 2016 and this will be used by government to review current advice on infant feeding to ensure it reflects the most up to date evidence.

The impact of the work of FSA on food allergy and food allergic consumers



Moira Austin

Helpline and Information Manager
Anaphylaxis Campaign

“The Anaphylaxis Campaign has worked closely with The Food Standards Agency for many years and we are immensely grateful to the FSA for its continued commitment to improving the lives of food allergic individuals and their families.

FSA's Food Allergy and Intolerance Research programme has been funding and continues to fund a wide range of vital research, including the ground-breaking EAT study.

The FSA's food allergy team are always ready to respond to specific allergen-related queries that may arise from our helpline or from food businesses that make

contact with us and provide expert insight into relevant issues facing the food industry related to severe allergies, associated research and advice on related policies and activities.

The work of the FSA has a huge and positive impact on food allergy and food allergic consumers and the Anaphylaxis Campaign is delighted and proud to work with them to help improve the lives of food allergic individuals and their families. The FSA's food allergy team is admired internationally. When meeting with other allergy patient organisations around the world they are impressed by, and envious of, the commitment of our National Agency.”

The preferences of those with food allergies and/or intolerances when eating out

University of Bath

This study will help the FSA and other relevant stakeholders understand the preferences and information seeking behaviours of those with food allergies and intolerances when eating out or buying foods not prepacked, for example, from a restaurant or a deli. It will also explore what impact the allergen rules in the Food Information Regulations (FIR) have on the quality of life of food allergic and intolerant consumers. This will inform relevant advice, guidance and tools for both consumers and food businesses to ensure safer food choices can be made confidently.

The first part of this study provided interesting insights into behaviours and

preferences of those with food allergy and intolerance, but also how they participate in social research projects. The study team found that some participants employed a 'Citizen Science' approach to investigate the information and service that was being provided to food allergic and intolerant consumers – actively seeking out restaurants and cafes to investigate and inform their views.

The second part of this study, which focusses on changes since the FIR was introduced in December 2014, is currently underway. The outcomes will be published next year.



What is the reach of FSA funded research?

It is important that FSA-funded research not only informs policy, but is also disseminated to a wide audience to help inform the research community around the world. It also makes consumers aware of advances in the understanding of food allergy and intolerance.

This year we have published work in highly respected scientific journals such as the New England Journal of Medicine and the BMJ and researchers have presented their work to audiences in the UK, the USA and in Europe.

The PIFA Study published a paper on food hypersensitivity in UK children in January 2016



The paper has been accessed over **2,000** times



It was reported on by **11** news outlets



Health professionals, journalists, members of public and scientists have tweeted about the findings

The findings of two FSA funded systematic reviews were published this year



The paper has been accessed over **44,000** times



There were over **160** news stories on the reviews



There have been **10** blogs and over **50** mentions on Facebook

The EAT Study published its findings in March 2016



The paper has been accessed over **132,000** times

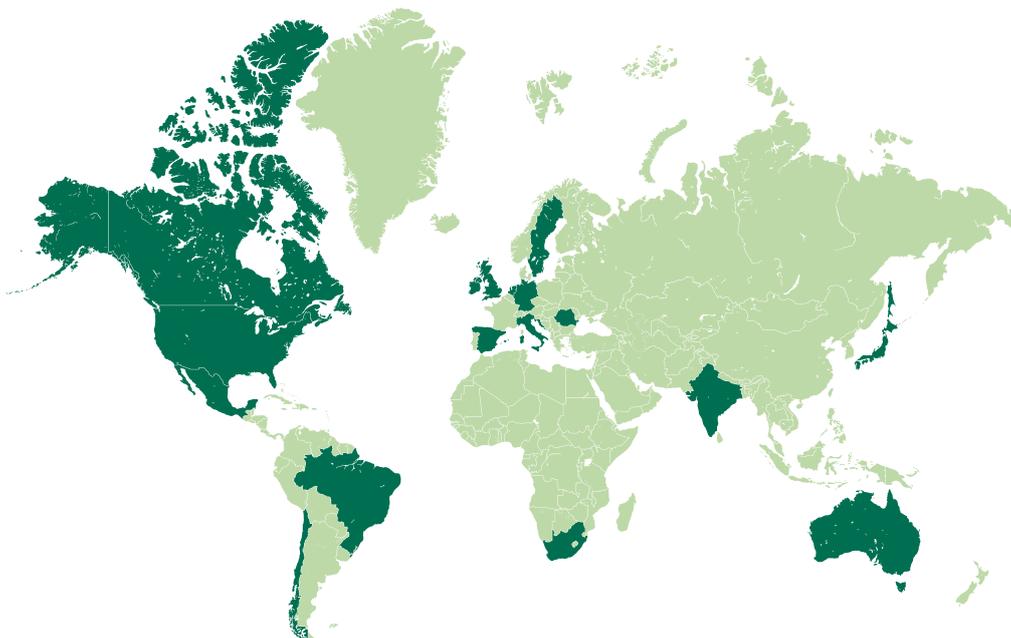


It was reported on by **92** news outlets



It has been cited by scientists almost **40** times

There has been international activity on Twitter in response to FSA-funded research – the countries in dark green show where people have tweeted about our research projects.¹



1. Data obtained from www.altmetric.com (accessed October 2016).

Food allergy incidents and risk assessment

In 2015, the FSA responded to over 200 food allergy incidents. The FSA is responsible for providing risk assessments which determine whether an incident poses a risk to food allergic or intolerant consumers and how severe that risk may be, as well as making recommendations for action to ensure the safety of consumers is maintained.

A recent incident involved the contamination of cumin; it was only due to a careful analysis, thorough investigation of the food supply chain, and use of innovation to respond to new risks that the true nature of the incident became known.

In January 2015, the FSA were made aware of an issue with the presence of undeclared nuts in cumin based products. Samples of ground cumin and cumin seed were collected from across the UK and market intelligence was used to focus on imports from particular countries and types of retailers.

Microscopy was used to analyse cumin seed and a technique called enzyme linked immunosorbent assay (ELISA) was used to

detect the presence of specific proteins in the samples.

ELISA showed that proteins from almonds were present in samples. However, the manufacturer could not identify how almond could have contaminated the cumin and suspicion then fell on a spice called mahaleb, which was ground on the same equipment as the cumin. The mahaleb (*Prunus mahaleb*) is from a closely related species to almond (*Prunus dulcis*) and therefore has very similar proteins. The ELISA test was unable to distinguish between them, giving a false positive result for almond.

A pioneering new DNA test was then developed by the UK's LGC, specialists in scientific measurement and testing. The test enabled the specific detection of mahaleb by identifying its unique characteristics.

This incident demonstrated that, whilst allergen detection methods are highly sensitive and an essential part of the risk assessment process, it is important for risk assessors to be aware of their limitations. There is a need to improve allergen detection methods for monitoring, surveillance and enforcement purposes.



Conclusion

Whilst there are differences between food allergy and food intolerance, they both represent a significant issue which affects the day-to-day lives of many consumers and their families. The FSA is aiming to improve the lives of food allergic and intolerant consumers and help them to make safe food choices by:

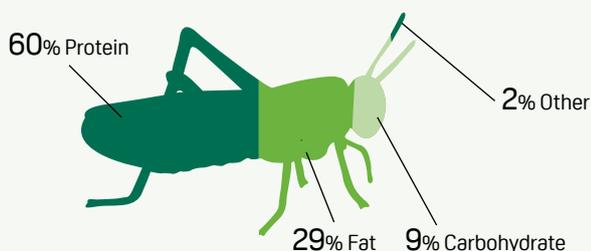
- commissioning ground breaking research to investigate key questions such as how food allergy may be prevented, and what factors affect the severity of an allergic reaction
- ensuring our research reaches a wide, international audience and is used to drive the evidence base forward
- using scientific approaches to provide risk assessments that protect consumers
- working closely with allergy support organisations to understand the needs of allergic consumers and ensure our research and advice reaches this audience



Also of interest: Bug bites – food of the future

It may seem unpalatable to some, but novel foods such as insects could be the sustainable food of the future. But what does this mean for food allergy?

With the growing world population, the demand for animal protein is predicted to increase by 75% between now and 2050, and insects are promising candidates as an alternative sustainable food source. Given the novelty of insects as food in Europe, there is a need to think more about potential food safety risks and how insects can be prepared and eaten safely. Along with physical, toxicological and microbiological risks, a key issue for any new sources of protein is the potential to cause food allergies.



Note: Typical composition on a dry weight basis.

From an allergy perspective the major risk associated with new foods like insects is that they can contain proteins that may elicit an allergic response in populations where they are newly introduced. This could be because the proteins are similar to existing allergens or because people become sensitised to the new proteins.

For insects, whilst this is an area where research is emerging, it is known they

can contain proteins that act as allergens that are common to all arthropods (mites, crustaceans, molluscs, etc.) The presence of these common proteins or pan-allergens can cause significant allergic reactions in some individuals. Recent research indicates that shrimp allergic individuals are highly likely to react to mealworms in the same way. A study in the Netherlands found that most of the shrimp-allergic individuals had a reaction to mealworm and developed moderate to severe symptoms. Tests on the IgE in these patients' blood showed they were reacting to, and therefore sensitised to, tropomyosin and arginine kinase, proteins that also occur in shrimp.

With a growing number of insect products appearing on the market it is important to consider how we balance getting the benefits of new foods while managing the risks for allergic consumers. Making consumers aware there is a potential for allergic reactions, especially for those with an allergy to crustaceans, will be an important step.

- In Thailand there are over 20,000 cricket farms.
- Worldwide grasshoppers, crickets and locusts are the most popular insects to eat.
- Insects are rich in protein, calcium, iron and have low fat and calorie content.

Acknowledgements

With thanks for the contributions from Liz Kendall, Jesús Alvarez-Piñera, Charlie Cameron, Chun-Han Chan, Ruth Willis, Sabrina Roberts, Ed Eaton and David Self.

We would also like to thank Professor Ian Kimber OBE for his continued support and expertise in his role as FSA Food Allergy and Intolerance Programme Adviser.

Further reading

Further information on completed and current FSA-funded research projects can be found on the FSA website: www.food.gov.uk/science/research/allergy-research

Committee on Toxicity statements on the influence of infant diet on the prevention of food allergy and other allergic and autoimmune conditions can be found at:

Hydrolysed formula:

<https://cot.food.gov.uk/sites/default/files/finalstatement-hydrolysedformula.pdf>

Timing of introduction of allergenic foods:

https://cot.food.gov.uk/sites/default/files/finalstatementontiming.doc_1.pdf

Further information on the risk assessment of mahaleb in cumin can be found at:

<https://www.gov.uk/government/news/cumin-analysis-dna-test-for-mahaleb-developed>

For more information, visit: food.gov.uk

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